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| 10/800,574 | 03/15/2004 | Vanessa I. Chinea | 82186688 | 1733 |

22879 7590 10/28/2011

HEWLETT-PACKARD COMPANY
Intellectual Property Administration
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| EXAMINER | |
|---|---|
| CRAWFORD, ERIK B | |
| ART UNIT | PAPER NUMBER |
| 1641 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 10/28/2011 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/800,574 | CHINEA, VANESSA I. | |
| | Examiner | Art Unit | |
| | Erik B. Crawford | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 August 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

5)☒ Claim(s) *1-10,19-24 and 26-33* is/are pending in the application.

5a) Of the above claim(s) *1-10 and 19-22* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *23,24 and 26-33* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *15 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims*

Claims 1-10, 19-24, and 26-33 are pending.

Claims 23, 24, and 26-33 are under examination.

Claims 1-10 and 19-22 are withdrawn.

Claims 11-18, 25 are cancelled.

Amendment to claims 1-3, 23, 24, 26, 31 and newly added claims 32 and 33 are acknowledged.

### *Withdrawn Objections and Rejections*

All previous objections and rejections, not reiterated herein, are withdrawn in view of Applicant's amendments and arguments filed 25 August 2011.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 23, 24, and 26-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Tokie** (US 6,513,897; already of record) and further in view of **Strickley** (*Pharmaceutical Research*, Vol. 21, No. 2, pages 201-230, February 2004; newly cited).

Independent claim 23 is drawn to a pharmaceutical dispensing apparatus, comprising:

a fluid dispenser, including:

a piezoelectric fluid ejection device or a thermal fluid ejection device; and

a fluid reservoir in fluid communication with the piezoelectric fluid ejection device or the thermal fluid ejection device; and

a pharmaceutical solution to be contained in the fluid reservoir and to be dispensed from the piezoelectric fluid ejection device or the thermal fluid ejection device, the pharmaceutical solution including an active pharmaceutical ingredient dissolved in a vehicle;

wherein the pharmaceutical solution has a viscosity i) ranging from about 1.15 cps to about 1.44 cps. or ii) of 2.6 cps. and a fluid surface tension (a) ranging from about 39 dynes/cm to about 49 dynes/cm. (b) ranging from about 46 dynes/cm to about 54 dynes/cm or (c) of about 62 dynes/cm;

wherein the viscosity and the fluid surface tension are selected so that the pharmaceutical solution is dispensed at a predetermined dosage within a variation of reproducibility of less than about 15%;

and wherein the vehicle is configured to, or exposed to conditions sufficient to substantially prevent instability of the active pharmaceutical ingredient during the dispensing of the pharmaceutical solution.

TOKIE teaches a piezoelectric or thermal fluid dispensing system for dispensing fluid material onto a substrate, wherein the fluid materials may include solvent-based solutions (as seen as applicant's instant vehicle) containing one or more additive components, which may include pharmaceutical compounds (Abstract; column 5, line 63 to col. 6 line 2; col. 6, lines 39-43; col. 9, lines 17-20 and 44-48). The ink jet 120 (e.g., piezoelectric or thermal) is supplied with jettable material 127 (e.g., a pharmaceutical solution) from a fluid reservoir 128 in fluid communication with the ink jet 120 (Figure 2; col. 6 lines 10-31). A typical fluid for thermal ink-jetting typically has a viscosity in the range of 3 to 5 centiPoise (col. 9, lines 12-13).

However, TOKIE is silent as to the desired fluid surface tension of the pharmaceutical solution.

STRICKLEY discloses oral and injectable solution formulations for solubilizing water-insoluble drugs for oral and injection administration (Abstract). Digoxin is one example of a practically water insoluble drug that necessitates the use of a solubilizing excipient, for example dimethylsulfoxide (DMSO), in order to solubilize the drug for oral or injection administration (page 204, Table I, 3rd listed molecule in left column; p. 209, Table II).

Therefore, it would have been *prima facie* obvious, to one of ordinary skill in the art, at the time the invention was made, to use digoxin as the pharmaceutical ingredient and DMSO as the vehicle, as taught by STRICKLEY, for the pharmaceutical solution in the apparatus of TOKIE.

One of ordinary skill in the art would have been motivated to incorporate digoxin and DMSO as the pharmaceutical solution in the apparatus of TOKIE in order to provide a solution in which digoxin is solubilized that can be coated onto a variety of substrates with increasing volumetric speeds using non-contact deposition techniques.

One of ordinary skill in the art would have a reasonable expectation of success in combining the teachings of TOKIE and STRICKLEY since TOKIE teaches using solvent-solutions comprising pharmaceutical compounds of non-contact deposition and STRICKLEY teaches the use of water-soluble organic solvents for solubilizing pharmaceutical compounds to be provided as oral or injectable formulations.

With respect to the specifically recited viscosities and fluid surface tensions in claim 23, TOKIE and STRICKLEY are both silent. However, when referring to claim 26 it is clear that the Applicant prefers digoxin as the pharmaceutical ingredient and DMSO as the vehicle. Thus, granted that STRICKLEY teaches digoxin as a pharmaceutical ingredient and DMSO as a vehicle it is asserted that the recited viscosity and fluid surface tension ranges would necessarily be achieved when combining the teachings of TOKIE and STRICKLEY.

With respect to the limitation in claim 23 of "…the viscosity and the fluid surface tension are selected so that…" this limitation constitutes an active method step and does not impart any additional structural features to the claimed apparatus. Therefore, provided that TOKIE and STRICKLEY disclose all of the structural features of the claimed apparatus it is asserted that a skilled artisan would be equally capable of

selecting specific viscosities and surface tensions of the pharmaceutical solution so that it is dispensed at a predetermined dosage within a variation of reproducibility of less than about 15%.

With respect to the specifically recited variation of reproducibility, TOKIE teaches accurate, reliable, and repeatable deposition of fluid materials (col. 8, line 66 to col. 8, line 2; col. 11, line 48-42), but does not specifically teach a variation of reproducibility of less than 15%. However, the recitation of "...a variation of reproducibility of less than about 15%," is considered an intended result that does not impart any additional structural features to the claimed apparatus. Therefore, provided that TOKIE in view of STRICKLEY disclose all of the structural features of the claimed apparatus it is asserted that their device is capable of achieving a variation of reproducibility of less than about 15%.

With respect to applicant's recitation of a,"…vehicle configured to, or exposed to conditions sufficient to substantially prevent instability of the active pharmaceutical ingredient (API)," in claim 23, TOKIE teaches pharmaceutical compounds as additives to fluid materials, which include solvent-based solutions, but does not explicitly discuss the solvent-based solution preventing instability of the API. However, the Applicant has stated that the vehicle into which the API is dissolved includes at least one solvent (page 9, line 15-16). Therefore, since TOKIE teaches pharmaceutical compounds in solvent-based solutions it is asserted that TOKIE meets the limitation of preventing instability of the API during dispensing.

With respect to claim 24, TOKIE teaches that the fluid dispensing system described above is able to achieve an approximate drop volume of 100 picoliters (col. 6, line 46). Furthermore, TOKIE teaches pharmaceutical compounds as additives to fluid materials, which would indicate that the pharmaceutical compound is present at some concentration within the low volume droplets. TOKIE does not explicitly teach that the API is highly concentrated.

However, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (MPEP 2144.05).

With respect to claim 26, as mentioned in the rejection of claim 23 above, STRICKLEY teaches digoxin as the pharmaceutical ingredient and DMSO as the vehicle.

With respect to claim 27, TOKIE teaches that the substrate onto which the droplets are dispensed may include one or more types of materials (e.g. papers, polymeric films, laminates, metals, etc.) (col. 4, lines 41-52). As mentioned above, the variation of reproducibility is considered an intended result that does not impart any additional structural features to the claimed apparatus. Furthermore, it has long been

settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable.

With respect to claims 27-30, as mentioned above, the various ranges of the variation of reproducibility are considered intended results that do no impart and additional structural features to the claimed apparatus. Therefore, since the apparatus disclosed by TOKIE in view of STRICKLEY contains all of the recited structural features of the claimed apparatus it is considered to be capable of achieving the intended results.

With respect to claim 31, TOKIE teaches a pharmaceutical compound as an additive to a solvent-based solution, but does not discuss the solubility of said compounds.

However, the solubility of a pharmaceutical compound is an inherent physical property that is directly related to the concentration of a pharmaceutical compound solution that can be prepared. The adjustment of particular conventional working conditions (e.g., determining result effective amounts of the ingredients beneficially taught by the cited references) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the artisan of ordinary skill. Accordingly, manipulation of the amounts of solute and solvent in the preparation of solutions for dispensing or testing would have been well within the purview of the person of ordinary skill in the art and no more than an effort to optimize results.

With respect to claim 32, TOKIE teaches that the reservoir 128 and/or fluid communication pathway 129 may be heated to supply the fluid material at a desired temperature and/or viscosity in order to ensure proper jetting of the material 127 (Figure 2; col. 6, lines 10-15). Although TOKIE does not explicitly teach that the heating is performed so that the stability of the pharmaceutical solution is unaffected, this recited limitation is considered an intended use. Since the apparatus taught by TOKIE is capable of heating the vehicle, it is asserted that it would be capable of doing so in order to maintain stability of the pharmaceutical solution.

With respect to claim 33, as mentioned above, STRICKLEY teaches DMSO as the vehicle.

Claims 23, 24, and 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over **TOKIE** and further in view of **Winnik *et al.*** (US 5,541,633; newly cited; hereinafter as "WINNIK").

With respect to claim 23, TOKIE teaches a piezoelectric or thermal fluid dispensing system for dispensing fluid material onto a substrate, wherein the fluid materials may include solvent-based solutions (as seen as applicant's instant vehicle) containing one or more additive components, which may include pharmaceutical compounds (Abstract; column 5, line 63 to col. 6 line 2; col. 6, lines 39-43; col. 9, lines 17-20 and 44-48). The ink jet 120 (e.g., piezoelectric or thermal) is supplied with jettable

material 127 (e.g., a pharmaceutical solution) from a fluid reservoir 128 in fluid communication with the ink jet 120 (Figure 2; col. 6 lines 10-31). A typical fluid for thermal ink-jetting typically has a viscosity in the range of 3 to 5 centiPoise (col. 9, lines 12-13).

However, TOKIE is silent as to the desired fluid surface tension of the pharmaceutical solution.

WINNIK teaches a thermal ink jet printing apparatus for dispensing a fluid (i.e. ink) onto a substrate (Abstract, col. 9, lines 31-35). The surface tension of the ink is preferably from about 25 to 45 dynes per square centimeter and the viscosity is preferably from about 1 to about 2.5 centiPoise (col. 11, lines 50-58; col. 12, lines 46-50).

Therefore, it would have been *prima facie* obvious, to one of ordinary skill in the art, at the time the invention was made, to use a pharmaceutical solution having the fluid material requirements (i.e. surface tension and viscosity) taught by WINNIK in the apparatus of TOKIE.

One of ordinary skill in the art would have been motivated to use a pharmaceutical solution having a viscosity and surface tension in the ranges taught by WINNIK as these are the preferred fluidic property requirements for fluids used in thermal ink jet printing, as suggested by WINNICK.

One of ordinary skill in the art would have a reasonable expectation of success in combining the teachings of TOKIE and WINNICK as bother references are drawn to thermal ink jet printers.

With respect to the limitation in claim 23 of "…the viscosity and the fluid surface tension are selected so that…" this limitation constitutes an active method step and does not impart any additional structural features to the claimed apparatus. Therefore, provided that TOKIE and STRICKLEY disclose all of the structural features of the claimed apparatus it is asserted that a skilled artisan would be equally capable of selecting specific viscosities and surface tensions of the pharmaceutical solution so that it is dispense at a predetermined dosage within a variation of reproducibility of less than about 15%.

With respect to the specifically recited variation of reproducibility, TOKIE teaches accurate, reliable, and repeatable deposition of fluid materials (col. 8, line 66 to col. 8, line 2; col. 11, line 48-42), but does not specifically teach a variation of reproducibility of less than 15%. However, the recitation of "...a variation of reproducibility of less than about 15%," is considered an intended result that does not impart any additional structural features to the claimed apparatus. Therefore, provided that TOKIE in view of STRICKLEY disclose all of the structural features of the claimed apparatus it is asserted that their device is capable of achieving a variation of reproducibility of less than about 15%.

With respect to applicant's recitation of a,"…vehicle configured to, or exposed to conditions sufficient to substantially prevent instability of the active pharmaceutical ingredient (API)," in claim 23, TOKIE teaches pharmaceutical compounds as additives to fluid materials, which include solvent-based solutions, but does not explicitly discuss

the solvent-based solution preventing instability of the API. However, the Applicant has stated that the vehicle into which the API is dissolved includes at least one solvent (page 9, line 15-16). Therefore, since TOKIE teaches pharmaceutical compounds in solvent-based solutions it is asserted that TOKIE meets the limitation of preventing instability of the API during dispensing.

Claims 24 and 27-32 are rejected under TOKIE in view of WINNIK for the reasons previously set forth in the rejection under TOKIE in view of STRICKLEY, since rejection of these claims are based on teachings of TOKIE.

Claims 26 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over **TOKIE** in view of **WINNIK** and further in view of **STRICKLEY**

TOKIE in view of WINNIK (combination hereinafter as "TOKIE") disclose a pharmaceutical dispensing apparatus, as described above.

However, TOKIE fails to disclose that the pharmaceutical ingredient is digoxin and the vehicle is DMSO.

With respect to claims 26 and 33, STRICKLEY discloses oral and injectable solution formulations for solubilizing water-insoluble drugs for oral and injection administration (Abstract). Digoxin is one example of a practically water insoluble drug that necessitates the use of a solubilizing excipient, for example dimethylsulfoxide (DMSO), in order to solubilize the drug for oral or injection administration (page 204, Table I, 3rd listed molecule in left column; p. 209, Table II).

Therefore, it would have been *prima facie* obvious, to one of ordinary skill in the art, at the time the invention was made, to use digoxin as the pharmaceutical ingredient and DMSO as the vehicle, as taught by STRICKLEY, for the pharmaceutical solution in the apparatus of TOKIE.

One of ordinary skill in the art would have been motivated to incorporate digoxin and DMSO as the pharmaceutical solution in the apparatus of TOKIE in order to provide a solution in which digoxin is solubilized that can be coated onto a variety of substrates with increasing volumetric speeds using non-contact deposition techniques.

One of ordinary skill in the art would have a reasonable expectation of success in combining the teachings of TOKIE and STRICKLEY since TOKIE teaches using solvent-solutions comprising pharmaceutical compounds for non-contact deposition and STRICKLEY teaches the use of water-soluble organic solvents for solubilizing pharmaceutical compounds to be provided as oral or injectable formulations.

## ***Response to Arguments***

Applicant's arguments with respect to claims 23, 24, and 26-31 have been considered but are moot in view of the new ground(s) of rejection.

## ***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Erik B. Crawford whose telephone number is (571)270-1011. The examiner can normally be reached on Monday through Friday, 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571)272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Erik B. Crawford/
Examiner, Art Unit 1641

/Melanie J Yu/
Primary Examiner, Art Unit 1641